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A cohort study of tobacco use, diet, occupation, and lung cancer mortality

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In 1966, a cohort of White males aged 35 or over, who were policy-holders with the Lutheran Brotherhood Insurance Society (United States), completed a mail questionnaire on tobacco use, diet, and demographic characteristics. During the 20 years of follow-up, 219 lung cancer deaths occurred. Besides the strong relationship with cigarette smoking, we observed an effect on lung cancer risk among current users of cigars or pipes who were nonsmokers of cigarettes (relative risk [RR] = 3.5, 95 percent confidence interval [CI] = 1.0-12.6) or who were past/occasional users of cigarettes (RR = 2.7, CI = 1.4-5.3). In addition, elevated risks (from 1.5 to 2.6) of lung cancer were found among craftsmen and laborers, with the highest risks among subjects who worked in the mining or manufacturing industry. No association between current (as of 1966) use of beer or hard liquor and lung cancer was observed, although past users were at elevated risk. An inverse association between lung cancer and intake of fruits was observed, and risks of lung cancer were lower among persons in the highest dietary intake quintiles of vitamins A and C. Except for oranges, however, none of the inverse associations with fruits or dietary nutrients had statistically significant trends. The findings from this cohort study add to the evidence of an adverse effect of cigar/pipe smoking and possibly protective effect of dietary factors on lung cancer risk.

Key words: Cohort study, diet, lung cancer, Lutheran Brotherhood study, occupation, United States.

Introduction

Lung cancer is the leading cause of cancer mortality among both men and women in the United States.[1] While as much as 90 percent of the lung cancer occurrence in men in this country may be attributed to cigarette smoking,[2] other exposures such as cigar and pipe smoking, occupation, and diet also play an etiologic role.[3-7] The current study, based on a cohort of 17,633 men whose mortality experience has been followed for 20 years, evaluates the role of tobacco use, occupation, and diet in lung cancer mortality.

Materials and methods

In 1966, 17,818 White male life-insurance policy-holders of the Lutheran Brotherhood Insurance Society (United States), who were 35 years of age or over, com-

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pleted a mail questionnaire, yielding a response rate of 68.5 percent. The respondents and nonrespondents were comparable in age, urban/rural residence, policy status, and cancer mortality at 11.5 years of follow-up.[8]

The questionnaire covered information on tobacco use, including the use of cigarettes, cigars, pipes, and smokeless tobacco. The occupation and industry in which the respondent had worked for the longest period of time also were elicited. Classification by major industries (mining/manufacturing, farming, and other, *i.e.*, service, transportation, trade, etc.) and occupational groups (professional/clerical, craftsman, laborer, and farm worker) was used for analysis. In addition, respondents were asked about the frequency of their current monthly consumption of 35 food items which were grouped for analysis into nine categories: meats, poultry, fish, eggs, dairy products, vegetables, cruciferous vegetables, fruits, and breads. The frequency of consumption of coffee, beer, and hard liquor also was ascertained.

Data from 185 respondents with more than 10 unknown responses to food items were excluded. Of 17,633 subjects available for final analysis, 71 percent had no missing data on any food items; 25 percent had fewer than five missing items; and four percent had between five and 10 missing food items. Intakes for the missing food items were imputed, using the median values of the remaining subjects, stratified by urban/rural residence, education, and age categories.

Nutrient intakes were computed using information on average portion size derived from the Second National Health and Nutrition Examination Survey (NHANES II)[9] and nutrient values from the US Department of Agriculture food consumption data.[10] Consumption of nutrients among cohort members was divided into quintiles, with approximately equal numbers of subjects in each intake stratum.

Underlying and contributory causes of death and other significant conditions were obtained from death certificates and coded by a nosologist at the Minnesota State Department of Health. By 1986, after 20 years and 286,731 person-years of follow-up, 4,513 deaths (26 percent of the cohort) had occurred. Another 4,027 subjects (23 percent) were lost to follow-up due to maturation or lapse of their policies. At 11.5 years of follow-up, no significant differences in age, urban/rural residence, vital status, and cause of death were detected between the active members and those who were lost to follow-up.[8]

Relative risks (RR) of lung cancer mortality were estimated for tobacco, occupation, and dietary variables using a Poisson regression program for modeling hazard functions with grouped data.[11,12] Person-years were accumulated up to death, loss to follow-up, or the end of the study in 1986. All RRs were age-adjusted using five-year intervals, and 95 percent confidence intervals (CI) were computed. Interactive effects between cigarette smoking and other exposure variables were examined. When appropriate, risk estimates were adjusted for smoking categories (never any tobacco; other tobacco only; occasional/past cigarette use; current daily cigarette use of 1-19, 20-29, 30+) and industry/occupational categories (service/trade: white collar worker, craftsman, laborer; mining/manufacturing: white collar worker, craftsman, laborer; and farm worker). For evaluation of the effect of coffee and alcohol consumption, additional categories were used to control for smoking (never any tobacco; other tobacco only; occasional/past daily cigarette use of 1-19, 20-29, 30+; current daily cigarette use of 1-19, 20-29, 30+).

Results

By 1986, 219 lung cancer deaths had occurred; 16 of these were reported as a contributing cause of death. Cigarette smoking was associated strongly with lung cancer death. Subjects who died of lung cancer were more than twice as likely to be current cigarette smokers in 1966 than the remaining cohort (65 percent *cf* 31 percent). Lung cancer death was not associated with marital status or urban/rural residence. Although the lung cancer subjects were less educated than the rest of the cohort, controlling for this variable did not affect the risk estimates after adjustment for age, cigarette smoking, and industry/occupation.

Among current cigarette smokers, the risk of lung cancer death increased substantially with the amount of consumption, with RRs ranging from 15.1 (CI = 5.9-38.4) for smokers of less than one pack per day to 48.4 (CI = 19.0-123.7) for those who smoked at least one and one-half packs per day (Table 1). Past/occasional cigarette smokers had a more than sixfold risk of lung cancer death (CI = 2.5-15.6) compared with nonusers of tobacco. Only one lung cancer subject used smokeless tobacco exclusively.

Persons who smoked pipes or cigars had more than a fourfold increase in risk of lung cancer death (CI = 1.2-14.9) (Table 1). The excess risk of lung cancer death in this group was detected mainly among current users of pipes/cigars (RR = 3.5, CI = 1.0-12.6). An excess was also seen for current pipe/cigar smokers who were past/occasional users of cigarettes (RR = 2.7, CI = 1.4-5.3) (Table 2). Among current cigarette smokers, no additional risk associated with pipe/cigar use was detected.

After adjustment for age and smoking status, differences by occupation remained (Table 3). Within each

Table 1. Relative risks (RR) of lung cancer mortality in relation to tobacco use in the Lutheran Brotherhood cohort, 1966-86

Tobacco use as of 1966	No. of deaths[a]	Person-years	RR[b]	CI[c]
Never any tobacco	5	58,888	1.0	—
Pipe/cigars only	5	13,677	4.3	1.2-14.9
Smokeless tobacco only	1	4,025	2.1	0.2-17.7
Cigarettes				
Past/occasional use[d]	63	107,450	6.3	2.5-15.6
Current daily use				
1-19	38	29,404	15.1	5.9-38.4
20-29	60	36,589	23.8	9.5-59.5
30+	40	15,732	48.4	19.0-123.7

[a] Subjects with missing information on tobacco use were excluded.
[b] Adjusted for age and industry/occupation; risks relative to non-users of any tobacco.
[c] CI = 95% confidence interval.
[d] Occasional users generally smoked less than one cigarette, pipe, or cigar per day.

Table 2. Relative risks (RR) of lung cancer mortality in relation to pipe/cigar smoking in the Lutheran Brotherhood cohort, 1966-86

Cigarette smoking as of 1966	Pipe/cigar smoking as of 1966	No. of deaths[a]	Person-years	RR[b]	CI[c]
Nonsmoker					
	None	6	63,279	1.0	—
	Past/occasional[d]	1	5,494	1.3	0.2-10.5
	Current	4	11,144	3.5	1.0-12.6
Past/occasional[d]					
	None	12	31,515	1.0	—
	Past/occasional[e]	14	34,648	1.0	0.5-2.2
	Current	33	35,940	2.7	1.4-5.3
Current[e]					
	None	45	25,647	1.0	—
	Past/occasional[d]	26	15,079	0.8	0.5-1.3
	Current	59	36,605	0.8	0.6-1.2

[a] Subjects with missing information on cigarette or pipe/cigar use were excluded.
[b] Adjusted for age and industry/occupation.
[c] CI = 95% confidence interval.
[d] Occasional smokers usually smoked less than one cigarette, pipe, or cigar per day.
[e] Further adjusted for pack-years of cigarette smoking (< 18, 18-32, > 32).

industry, craftsmen had a twofold or higher risk of lung cancer death relative to white collar workers, with

Table 3. Relative risks (RR) of lung cancer mortality by industry/occupation in the Lutheran Brotherhood cohort, 1966-86

Industry[a]	Occupation[a]	No. of deaths[b]	Person-years	RR[c]	CI[d]
Service/trade	White collar	37	81,708	1.0[e]	—
	Craftsman	13	12,606	2.0	1.1-3.7
	Semi-skilled/laborer	12	12,046	1.5	0.8-2.9
Mining/manufacturing	White collar	14	25,443	1.2	0.7-2.3
	Craftsman	48	32,252	2.6	1.7-4.1
	Semi-skilled/laborer	24	18,335	2.3	1.4-3.8
Agriculture	Farm worker	55	89,991	1.3	0.9-2.0

[a] Industry and occupation held for the longest period of time as of 1966.
[b] Subjects with missing information on industry or occupation were excluded.
[c] Adjusted for age and smoking status; risks relative to white-collar workers in service/trade industry.
[d] CI = 95% confidence interval.
[e] Reference category.

the risk for laborers elevated to a lesser extent. Differences between the major industries were small. Farm workers had a 30 percent excess risk of lung cancer relative to white-collar service workers, although this increase was not statistically significant.

Risk of lung cancer according to beverage intake is shown in Table 4. Lung cancer risk increased with the amount of coffee consumed. Consumption of three to four cups of coffee per day was associated with about a twofold increased lung cancer risk, and doubling intake to seven or more cups had little additional effect. The excess risk was observed almost entirely among current cigarette smokers; among nonsmokers or past smokers, no increased risk with coffee drinking was detected (data not shown). No significant trend was found between lung cancer and current use (as of 1966) of beer or hard liquor (Table 4). An elevated risk of lung cancer was observed, however, among former drinkers of beer (adjusted RR = 1.8, CI = 1.1-3.0) and hard liquor (adjusted RR = 1.9, CI = 1.1-3.1). Exclusion of the first five years of follow-up did not materially alter the results with regard to coffee, beer, or hard liquor consumption.

Examination of diet by food groups (Table 5) revealed a mild reduction in risk of lung cancer with higher intake of fruits, and lesser reductions in risk for cruciferous vegetables and dairy products. Individual food items that were linked to a lower risk of lung cancer death included oranges, apples, grapes, canned

Table 4. Relative risks of lung cancer mortality in relation to coffee and alcohol use in the Lutheran Brotherhood cohort, 1966-86

Beverage use as of 1966	No. of deaths[a]	Person-years	RR[b]	CI[c]
Coffee (cups/day)				
< 3	27	87,784	1.0	----
3-4	96	107,580	2.1	1.4-3.2
5-6	62	63,464	2.1	1.3-3.3
> 6	33	26,490	2.4	1.4-4.2
Beer (times/month)				
Never used	29	72,077	1.0	—
< 3	66	91,614	1.2	0.8-1.9
3-5	31	39,099	1.4	0.8-2.3
6-13	31	28,601	1.7	1.0-2.9
> 13	25	29,818	1.1	0.6-1.9
Used before	31	19,763	1.8	1.1-3.0
Hard liquor (times/month)				
Never used	38	89,118	1.0	—
< 3	83	100,460	1.3	0.9-2.0
3-5	28	31,179	1.3	0.8-2.1
6-13	22	22,218	1.3	0.7-2.2
> 13	16	19,693	1.0	0.5-1.8
Used before	28	16,522	1.9	1.1-3.1

[a] Subjects with missing information on coffee, beer, or whisky use were excluded from the respective category.
[b] Adjusted for age, industry/occupation, and smoking status.
[c] CI = 95% confidence interval.

Table 5. Relative risks (RR) of lung cancer mortality in relation to intake of food groups in the Lutheran Brotherhood cohort, 1966-86

Foods groups[a] (time/month)	No. of deaths	Person-years	RR[b]	CI[c]
Meat				
< 16	38	50,613	1.0	—
16-45	137	190,050	1.1	0.8-1.6
46-75	29	30,667	1.4	0.9-2.4
> 75	15	15,748	1.3	0.7-2.3
Poultry				
< 4	105	133,120	1.0	—
4-8	77	109,660	0.9	0.7-1.2
9-13	25	22,501	1.4	0.9-2.2
> 13	12	21,797	0.7	0.4-1.2
Fish				
< 2	39	62,477	1.0	—
2-4	119	152,420	1.2	0.9-1.8
5-15	51	60,618	1.2	0.8-1.8
> 15	10	11,562	1.0	0.5-2.1
Eggs				
< 10	55	66,760	1.0	----
10-18	66	90,148	0.9	0.6-1.3
19-30	64	80,963	1.0	0.7-1.4
> 31	34	49,211	0.9	0.6-1.3
Dairy				
< 46	131	139,970	1.0	—
46-95	60	87,448	0.9	0.6-1.2
96-142	16	31,329	0.9	0.5-1.5
> 142	12	28,334	0.8	0.4-1.4
Bread				
< 91	54	76,152	1.0	—
91-150	81	92,378	1.2	0.8-1.7
151-240	58	85,915	0.9	0.6-1.3
> 240	26	32,638	1.0	0.6-1.7
Vegetables				
< 46	29	34,985	1.0	—
46-90	117	154,340	1.1	0.7-1.7
91-160	60	82,988	1.1	0.7-1.8
> 160	13	14,767	1.2	0.6-2.3
Cruciferous vegetable				
< 2	43	58,455	1.0	—
2-4	112	146,730	0.9	0.6-1.3
5-8	46	56,035	1.0	0.7-1.5
> 8	18	25,861	0.8	0.5-1.4
Fruit				
< 31	74	73,335	1.0	—
31-60	86	121,340	0.8	0.6-1.1
61-90	42	64,565	0.8	0.5-1.2
> 90	17	27,837	0.7	0.4-1.3

[a] Frequency of intake in 1966.
[b] Adjusted for age, smoking status and industry/occupation.
[c] CI = 95% confidence interval.

fruits, fruit juices, carrots, rutabaga, cauliflower, corn, and eggs (data not shown). Except for oranges, however, none of the inverse associations with food items or food groups had statistically significant trends, after adjustment for age, smoking status, and industry/occupation. Consumption of more than 14 servings of oranges per month was associated with a 30 percent reduction in lung cancer risk (P for trend < 0.01).

Dietary intake of vitamin A and its components generally was associated with lowered risk of lung cancer, with persons in the highest intake-level of vitamin A, β-carotene, or total carotenoids having a 20 percent reduction in risk (Table 6). Intake of vitamin C also was associated with a reduced risk of lung cancer death. However, the trends for reduced risk with these associations were not consistent and did not reach statistical significance. No consistent effect modification was detected between intake of vitamin C and vitamin A or its components, and between these micronutrients and cigarette smoking. Intake of total fat, saturated fat, or cholesterol—after adjustment for age, industry/occupation, and smoking status—was not related to lung cancer risk (data not shown). Further adjustment for caloric intake did not alter the risk estimates appreciably.

Table 6. Relative risks (RR) of lung cancer mortality in relation to dietary nutrient intake in the Lutheran Brotherhood cohort, 1966-86

Dietary nutrient	Intake quintiles[a]	No. of deaths	Person-years	RR[b]	CI[c]
Vitamin A	1 Low	60	55,751	1.0	—
	2	39	57,772	0.8	0.5-1.1
	3	45	58,161	0.9	0.6-1.4
	4	42	57,725	1.0	0.6-1.4
	5 High	33	57,672	0.8	0.5-1.2
Total retinol	1 Low	52	55,329	1.0	—
	2	53	57,038	1.1	0.8-1.7
	3	50	57,603	1.2	0.8-1.8
	4	32	58,335	0.8	0.5-1.3
	5 High	32	58,776	0.9	0.6-1.4
Total carotenoids	1 Low	54	56,978	1.0	—
	2	45	57,770	1.0	0.6-1.4
	3	40	58,091	0.8	0.6-1.3
	4	45	57,739	1.1	0.7-1.6
	5 High	35	56,504	0.8	0.5-1.2
β-carotene	1 Low	54	57,121	1.0	—
	2	38	57,527	0.8	0.5-1.1
	3	45	58,188	1.0	0.7-1.5
	4	47	57,170	1.0	0.7-1.5
	5 High	35	57,076	0.8	0.5-1.2
Vitamin C	1 Low	64	56,400	1.0	—
	2	39	57,870	0.7	0.5-1.1
	3	45	58,070	0.9	0.6-1.4
	4	33	57,788	0.7	0.4-1.0
	5 High	38	56,954	0.8	0.5-1.2

[a] Based on dietary intakes in 1966.
[b] Adjusted for age, industry/occupation, and smoking status.
[c] CI = 95% confidence interval.

Discussion

Our findings of (i) a large increase in risk of lung cancer with amount of cigarettes smoked; (ii) an increased risk in cigar/pipe smokers and in persons who held jobs as craftsmen or laborers; and (iii) a protective effect suggested for fruits and higher dietary intakes of vitamins A and C are consistent with results from previous investigations, including an earlier report on this cohort after only 10 years of follow-up.[13] Because of the prospective nature of the study, exposure information ascertained in this study was not subject to recall or other selective biases in reporting,[14] and adds to the existing body of evidence regarding these issues.

Limitations in the current data should be considered in interpreting the results. A number of food items that are rich in vitamins A and C such as cheese, liver, broccoli, spinach, and cantaloupe were not included in the quesionnaire developed in 1966. The resulting misclassifications in intakes of these nutrients generally would lead to underestimates of the true effects. In addition, almost 30 percent of the subjects had missing information on at least one food item, so that intakes for these missing foods were imputed. It can be estimated, however, that the imputed values contributed to less than four percent of any one nutrient intake. Furthermore, the imputation using the median values of the remaining subjects generated conservative estimates of true intakes. Therefore, the true effects of dietary nutrients on lung cancer might be underestimated.

Since the initial data collection in 1966, our agreement with the Lutheran Brotherhood Insurance Society prevented further direct contact with the cohort members for updated exposure information. If this cohort follows general trends among American men, a substantial proportion of the cohort members would have stopped cigarette smoking during the 20 years of follow-up.[2,15] Despite the likely misclassification of post-1966 quitters as current smokers, which should lower risk over time, estimates of RR of lung cancer among smokers in fact increased somewhat by each successive five years of cumulative follow-up.

About 23 percent of the cohort members were lost to follow-up. We examined the demographic and exposure variables of the active members and those lost to follow-up at 20 years and found them to be similar. Moreover, a special study to review the vital status and cause-of-death of those lost to follow-up at 11.5 years detected no significant difference in mortality between these two groups.[8] Thus, we have evidence to indicate that the loss-to-follow-up is unlikely to have biased the study results.

Because the cohort members were restricted to White men who held a life insurance policy, the generalizability of the results may be limited. While there is no reason to believe that the risk factors identified in the current study affect these men exclusively, the patterns of associations and relative contribution of these risk factors to lung cancer mortality may differ in other populations.

The excess of lung cancer associated with cigar/pipe smoking adds to the evidence of carcinogenic risk, independent of the effects of cigarette smoking.[3,4,16] The increased risk associated with cigar/pipe smoking was limited to nonsmokers and past/occasional smokers of cigarettes. The failure to detect an effect of cigar/pipe smoking among current cigarette smokers may be related to a dominating influence of cigarette smoking and/or to the observation that mixed smokers tend to inhale cigarette smoke less frequently and less deeply than cigarette-only smokers.[4] While earlier studies have reported an elevated risk of lung cancer among former exclusive cigar/pipe smokers,[3] the present study failed to detect such an effect, although the

power to assess moderate increases in risk was low. Detailed information on age started and stopped smoking and amount smoked was not ascertained for pipe and cigar use, so more detailed evaluation of risk among current and past users of these tobacco products could not be made.

A variety of industrial exposures have been associated with lung cancer in previous investigations, including asbestos (*e.g.*, insulation and shipyard workers), radon (miners), polycyclic hydrocarbons (gas workers, coke-oven workers and roofers), chromium (chromate workers), nickel (refinery workers), mustard gas (mustard factory workers), bischloromethyl ether (chemical workers), and inorganic arsenic (copper smelter workers, and pesticide and herbicide workers).[5,17,18] Our finding of a higher risk of lung cancer in craftsmen and laborers relative to white collar workers, especially for persons in the mining or manufacturing industries, is not as specific but generally is consistent with earlier findings. Because of the small number of observations, however, risk by individual industry and occupation was not possible. Also, lifetime occupation was not ascertained in the questionnaire, only occupation held for the longest period of time as of 1966.

In most previous studies, farmers were found to have a reduced risk of lung cancer.[19-21] Our observation of a slight excess in lung cancer risk among farmers may be explained, in part, by the relatively low lung cancer deaths in the reference occupation group (*i.e.*, white-collar service/trade workers) and by our detailed adjustment for tobacco use. Since pesticide use has been linked to lung cancer,[18,22] and farmers often may be exposed to these chemicals,[23] further investigation may be warranted to evaluate whether certain occupational exposures in the farming industry may be associated with an excess risk of lung cancer.

A cohort study in Norway[24] found no association of lung cancer with coffee drinking after adjustment for cigarette smoking, but there have been some other reports of a slightly elevated risk of lung cancer among heavy coffee drinkers,[25,26] including a preliminary report based on 17.5 years follow-up of the Lutheran Brotherhood cohort.[27] Because cigarette smoking and coffee are so highly correlated and the excess risk among coffee drinkers was confined to current cigarette smokers, much of the association with coffee appears due to residual confounding by smoking.

Alcohol use has been linked with lung cancer in some studies, but most of the reported associations may be explained by confounding due to lack of adjustment for cigarette smoking or residual confounding by smoking.[28-30] Our findings do not support an association between lung cancer and amount of beer or hard liquor use, although an excess risk of lung cancer was found among ex-drinkers of beer or hard liquor. These former drinkers did not report heavier cigarette smoking than current drinkers. However, it is possible that factors related to discontinuation of drinking alcohol, such as poor health, also may be associated with higher risk of lung cancer. Since the date and reason for stopping alcohol use were not elicited, the current study could not address these issues. Exclusion of the first five years of follow-up, however, did not alter the risk estimates appreciably for past use of beer or hard liquor.

A few ecologic[31-33] and case-control[34-37] studies have suggested a role for dietary fat or cholesterol in the development of lung cancer, although other studies have shown no relationship.[38,39] The risk reported for dietary cholesterol or fat intake was detected only among males,[35-37] heavy current smokers,[35] or only in the highest intake quartile of cholesterol.[34] An earlier cohort study[39] did not find an excess risk of lung cancer with high intake of dietary cholesterol, while another recent cohort study reported an association with cholesterol intake from eggs only.[40] The current cohort data do not support an association between fat, cholesterol, or egg intake and lung cancer, although the sources of fat or cholesterol in our data are limited as there were no questions on frequency of use of butter, margarine, cheese, oils, or food preparation methods.

Since Bjelke[41] first reported a much-reduced rate of lung cancer among Norwegian men with above average intakes of vitamin A from mostly plant sources, a large body of evidence has been accumulated on the potential protective effect of carotenoids on lung cancer.[7,34,37,42-50] The current study also revealed a mildly reduced risk of lung cancer with highest intake of vitamin A, β-carotene and total carotenoids. Our failure to observe associations as strong as those reported in some previous investigations,[37,44,45,47-49] may be due, in part, to the limited number of food sources for this vitamin in the questionnaire.

Recently, a reduced risk of lung cancer in relation to higher intake of vitamin C has been reported,[7,46,49] although this association was not detected in several earlier investigations.[7,37,47] Our results suggest that vitamin C may have a protective effect on lung cancer independent of that of vitamin A. Part of the observed trend with vitamin C results from the protective effect with intake of oranges. A strong protective effect of fruit intake on lung cancer also has been reported in two cohort studies.[51,52] While a major component of the protective effect of fruit intake may be derived from vitamin C due to its antioxidant and other functions,[53] the potential antitumor effect of other nutritional components of fruit also should be explored in future studies.

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